

Serial No.: 08/999,690

IN THE CLAIMS:

221 AUG 26 PM 2:36

Please amend the claims as follows:

1. (Currently amended) A recombinant retroviral vector comprising, in operable linkage,
 - (a) retroviral vector DNA or at least a portion of the retroviral vector DNA comprising elements necessary for infection and direction of expression in target cells; and
 - (b) one or more coding sequences which encode a ~~naturally occurring~~ therapeutic antimicrobial peptide ~~or a biologically active derivative thereof~~, wherein the antimicrobial peptide ~~or derivative thereof~~ is selected from the group consisting of: melittin, ~~premelittin, prepromelittin, cecropin, prececropin, preprocecropin, magainin, a part thereof, an analogue thereof, a homologue thereof a preform thereof, a preproform thereof, a biologically active peptide derived therefrom and a combination thereof.~~
2. (Currently amended) A recombinant retroviral vector comprising in operable linkage,
 - (a) a 5' long terminal repeat region comprising the structure U3-R-U5;
 - (b) one or more ~~of said~~ coding sequences wherein at least one sequence encodes for a ~~naturally occurring~~ therapeutic antimicrobial peptide ~~or a biologically active derivative thereof~~, wherein the antimicrobial peptide ~~or derivative thereof~~ is selected from the group consisting of: melittin, ~~premelittin, prepromelittin, cecropin, prececropin, preprocecropin, magainin, a part thereof, an analogue thereof, a homologue thereof a preform thereof, a preproform thereof, a biologically active peptide derived therefrom and a combination thereof; and~~
 - (c) a 3' long terminal repeat region comprising a completely or partially deleted U3 region wherein said deleted U3 region is replaced by a

Serial No.: 08/999,690

202 116 86 Pw 2 27

polylinker sequence, followed by the R and U5 region to undergo promoter conversion.

3. (Canceled)
4. (Original) The recombinant vector according to Claim 2, wherein said polylinker sequence comprises at least one unique restriction site and, optionally, at least one insertion of a heterologous DNA fragment.
5. (Currently amended) A recombinant retroviral vector comprising in operable linkage,
 - (a) a 5' long terminal repeat region comprising the structure U3-R-U5;
 - (b) one or more coding sequences wherein at least one sequence encodes for at least one ~~naturally occurring therapeutic antimicrobial peptide or a biologically active derivative thereof~~, wherein the antimicrobial peptide or derivative thereof is selected from the group consisting of: melittin, premelittin, prepremelittin, cecropin, prececcropin, preproceccropin, magainin, ~~a part thereof, an analogue thereof, a homologue thereof a preform thereof, a preproform thereof, a biologically active peptide derived therefrom and a combination thereof; and~~
 - (c) a 3' long terminal repeat region comprising a completely or partially deleted U3 region wherein said deleted U3 region is replaced by a polylinker sequence which comprises at least one unique restriction site and at least one insertion of a heterologous DNA fragment which regulates the expression of at least one of the coding sequences of said vector, and comprises at least one or more elements selected from the group consisting of: regulatory elements and promoters.
6. (Previously presented) The recombinant retroviral vector according to Claim 1 further comprising at least one non-coding sequence selected from the group

- consisting of: regulatory elements and promoters, which regulate the expression of at least one of the coding sequences.
7. (Previously presented) The recombinant retroviral vector according to Claim 6, wherein said regulatory elements and promoters are regulatable by transacting molecules.
 8. (Previously presented) The recombinant retroviral vector according to Claim 4, wherein said heterologous DNA fragment encodes a peptide selected from the group consisting of marker peptides, therapeutic peptides, cell cycle regulatory peptides, tumor suppressor peptides, antiproliferation peptides and cytokines.
 9. (Currently amended) A recombinant retroviral vector system comprising:
 - (a) a recombinant vector comprising, in operable linkage,
 - (i) retroviral vector DNA or at least a portion of the retroviral vector DNA comprising elements necessary for infection and direction of expression in target cells; and
 - (ii) one or more coding sequences wherein at least one sequence encodes for a ~~naturally occurring~~ therapeutic antimicrobial peptide ~~or a biologically active derivative thereof~~, wherein the antimicrobial peptide ~~or derivative thereof~~ is selected from the group consisting of: melittin, ~~premelittin, prepromelittin, cecropin, prececcropin, preproceccropin, magainin, a part thereof, an analogue thereof, a homologue thereof a preform thereof, a preproform thereof, a biologically active peptide derived therefrom~~ and a combination thereof; and
 - (b) a packaging cell line harboring at least one retroviral construct coding for proteins required for said retroviral vector to be packaged.

Serial No.: 08/999,690

10. (Original) The recombinant retroviral vector system according to Claim 9, wherein said retroviral vector comprises, in operable linkage,
- (a) a 5' long terminal repeat region comprising the structure U3-R-U5;
 - (b) one or more of said coding sequences; and
 - (c) a 3' long terminal repeat region comprising a completely or partially deleted U3 region wherein said deleted U3 region is replaced by a polylinker sequence, followed by the R and U5 region to undergo promoter conversion.
11. (Currently amended) A retroviral particle produced by the recombinant retroviral vector system according to Claim [[9]] 10 after transfecting the packaging cell line with the retroviral vector.
12. (Currently amended) A retroviral provirus produced by infection of target cells with a recombinant retroviral particle according to Claim 11 whereby the U3 sequence region is duplicated during the process of reverse transcription in the infected target cell and appears in the 5' long terminal repeat and the 3' long terminal repeat of the resulting provirus, and the U5 of the 5' long terminal repeat is duplicated during the process of reverse transcription in the infected target cell and appears in the 3' long terminal repeat and in the 5' long terminal repeat of the resulting provirus.
13. (Original) The retroviral provirus of Claim 12 wherein said polylinker comprises heterologous DNA.
14. (Previously presented) A method for introducing nucleotide sequences into an isolated cell population comprising infecting the cell population with the recombinant retroviruses produced by the recombinant retroviral vector system according to Claim 9.

Serial No.: 08/999,690

15. (Original) The method of Claim 14 wherein the cell population is selected from the group consisting of: human cells and animal cells.

16-19. (Canceled)

20. (Currently amended) A mRNA of a retroviral provirus produced by infection of target cells with a recombinant retroviral particle from a recombinant retroviral vector system comprising:

- (a) a recombinant vector comprising, in operable linkage,
 1. retroviral vector DNA or at least a portion of the retroviral vector DNA comprising elements necessary for infection and direction of expression in target cells; and
 2. one or more coding sequences wherein at least one sequence encodes for a naturally occurring therapeutic antimicrobial peptide ~~or a biologically active derivative thereof~~, wherein the antimicrobial peptide ~~or derivative thereof~~ is selected from the group consisting of: melittin, ~~premelittin, prepromelittin,~~ cecropin, ~~prececropin, preprocecropin,~~ magainin, ~~a part thereof, an analogue thereof, a homologue thereof a preform thereof, a preproform thereof, a biologically active peptide derived therefrom~~ and a combination thereof; and
 - (b) a packaging cell line harboring at least one retroviral construct coding for proteins required for said retroviral vector to be packaged.
21. (Currently amended) A RNA produced by a recombinant retroviral vector wherein said vector comprises, in operable linkage,
 - (a) retroviral vector DNA or at least a portion of the retroviral vector DNA comprising elements necessary for infection and direction of expression in target cells; and

- (b) one or more coding sequences wherein at least one sequence encodes for a naturally occurring therapeutic antimicrobial peptide or a biologically active derivative thereof, wherein the antimicrobial peptide or derivative thereof is selected from the group consisting of: melittin, ~~premelittin, prepromelittin, cecropin, prececcropin, preprocceccropin, magainin, a part thereof, an analogue thereof, a homologue thereof a preform thereof, a preproform thereof, a biologically active peptide derived therefrom and a combination thereof.~~
22. (Previously presented) An isolated host cell infected with a virion according to Claim 11.
- 23-25. (Canceled)
26. (Previously presented) A non-human host cell infected with a virion according to Claim 11.
27. (Currently amended) A recombinant retroviral vector comprising, in operable linkage,
- (a) retroviral vector DNA or at least a portion of the retroviral vector DNA comprising elements necessary for infection and direction of expression in target cells; and
- (b) one or more coding sequences which encode a naturally occurring therapeutic antimicrobial peptide or a biologically active derivative thereof, wherein the antimicrobial peptide or derivative thereof is selected from the group consisting of: melittin, ~~premelittin, prepromelittin, a part thereof, an analogue thereof, a homologue thereof a preform thereof, a preproform thereof, a biologically active peptide derived therefrom, and a combination thereof.~~

Serial No.: 08/999,690

28. (Currently amended) A recombinant retroviral vector comprising in operable linkage,

- (a) a 5' long terminal repeat region comprising the structure U3-R-U5;
- (b) one or more of said coding sequences wherein at least one sequence encodes for a ~~naturally occurring therapeutic antimicrobial peptide or a biologically active derivative thereof~~, wherein the antimicrobial peptide ~~or derivative thereof~~ is selected from the group consisting of: melittin, premelittin, prepromelittin, a part thereof, an analogue thereof, a homologue thereof a preform thereof, a preproform thereof, a biologically active peptide derived therefrom, and a combination thereof; and
- (c) a 3' long terminal repeat region comprising a completely or partially deleted U3 region wherein said deleted U3 region is replaced by a polylinker sequence, followed by the R and U5 region to undergo promoter conversion.

29. (Canceled)

30. (Previously presented) The recombinant retroviral vector according to Claim 28, wherein said polylinker sequence comprises at least one unique restriction site and, optionally, at least one insertion of a heterologous DNA fragment.

31. (Currently amended) A recombinant retroviral vector comprising in operable linkage,

- (a) a 5' long terminal repeat region comprising the structure U3-R-U5;
- (b) one or more of said coding sequences wherein at least one sequence encodes for a ~~naturally occurring therapeutic antimicrobial peptide or a biologically active derivative thereof~~, wherein the antimicrobial peptide ~~or derivative thereof~~ is selected from the group consisting of: melittin, premelittin, prepromelittin, a part thereof, an analogue thereof, a

- ~~homologue thereof a preform thereof, a preproform thereof, a biologically active peptide derived therefrom, and a combination thereof; and~~
- (c) a 3' long terminal repeat region comprising a completely or partially deleted U3 region wherein said deleted U3 region is replaced by a polylinker sequence which comprises at least one unique restriction site and at least one insertion of a heterologous DNA fragment which regulates the expression of at least one of the coding sequences of said vector, and comprises at least one or more elements selected from the group consisting of: regulatory elements and promoters.

32-33. (Canceled)

34. (Previously presented) The recombinant retroviral vector according to Claim 30, wherein said heterologous DNA fragment encodes a peptide selected from the group consisting of marker peptides, therapeutic peptides, cell cycle regulatory peptides, tumor suppressor peptides, antiproliferation peptides and cytokines.
35. (Currently amended) A recombinant retroviral vector system comprising:
- (a) a recombinant vector comprising, in operable linkage,
- (i) retroviral vector DNA or at least a portion of the retroviral vector DNA comprising elements necessary for infection and direction of expression in target cells; and
- (ii) one or more coding sequences wherein at least one sequence encodes for at least one ~~naturally occurring~~ therapeutic antimicrobial peptide ~~or a biologically active derivative thereof~~ wherein the antimicrobial peptide ~~or derivative thereof~~ is selected from the group consisting of: melittin, ~~premelittin, prepromelittin, a part thereof, an analogue thereof, a homologue thereof a~~

preform thereof, a preproform thereof, a biologically active peptide derived therefrom, and a combination thereof; and

- (b) a packaging cell line harboring at least one retroviral construct coding for proteins required for said retroviral vector to be packaged.
36. (Previously presented) The recombinant retroviral vector system according to Claim 35, wherein said retroviral vector comprises, in operable linkage,
- (a) a 5' long terminal repeat region comprising the structure U3-R-U5;
 - (b) one or more of said coding sequences; and
 - (c) a 3' long terminal repeat region comprising a completely or partially deleted U3 region wherein said deleted U3 region is replaced by a polylinker sequence, followed by the R and U5 region to undergo promoter conversion.
37. (Currently amended) A retroviral particle produced by the recombinant retroviral vector system according to Claim [[35]] 36 after transfecting the packaging cell line with the retroviral vector system.
38. (Currently amended) A retroviral provirus produced by infection of target cells with a recombinant retroviral particle according to Claim 37 whereby the U3 sequence region duplicated during the process of reverse transcription in the infected target cell and appears in the 5' long terminal repeat and the 3' long terminal repeat of the resulting provirus, and the US of the 5' long terminal repeat duplicated during the process of reverse transcription in the infected target cell and appears in the 3' long terminal repeat and in the 5' long terminal repeat of the resulting provirus.
39. (Previously presented) The retroviral provirus of Claim 38 wherein said polylinker comprises heterologous DNA.

Serial No.: 08/999,690

40. (Previously presented) A method for introducing nucleotide sequences into an isolated cell population comprising infecting the cell population with the recombinant retroviruses produced by the recombinant retroviral vector system according to Claim 35.

41-45. (Canceled)

46. (Currently amended) A mRNA of a retroviral provirus produced by infection of target cells with a recombinant retroviral particle from a recombinant retroviral vector system comprising:

- (a) a recombinant vector comprising, in operable linkage
 - (i) a retroviral vector DNA or at least a portion of the retroviral vector DNA comprising elements necessary for infection and direction of expression in target cells; and
 - (ii) one or more coding sequences wherein at least one sequence encodes for at least one naturally occurring therapeutic antimicrobial peptide ~~or a biologically active derivative thereof~~ wherein the antimicrobial peptide ~~or derivative thereof~~ is selected from the group consisting of: melittin, ~~premelittin, prepromelittin, a part thereof, an analogue thereof, a homologue thereof a preform thereof, a preproform thereof, a biologically active peptide derived therefrom, and a combination thereof;~~ and
- (b) a packaging cell line harboring at least one retroviral construct coding for proteins required for said retroviral vector to be packaged.

47. (Currently amended) A RNA produced by a vector recombinant retroviral vector system comprising:

- (a) a recombinant vector comprising, in operable linkage,

Serial No.: 08/999,690

- (i) retroviral vector DNA or at least a portion of the retroviral vector DNA comprising elements necessary for infection and direction of expression in target cells; and
 - (ii) one or more coding sequences wherein at least one sequence encodes for at least one ~~naturally occurring~~ therapeutic antimicrobial peptide ~~or a biologically active derivative thereof~~ wherein the antimicrobial peptide ~~or derivative thereof~~ is selected from the group consisting of: melittin, ~~premelittin, prepromelittin, a part thereof, an analogue thereof, a homologue thereof a preform thereof, a preproform thereof, a biologically active peptide derived therefrom,~~ and a combination thereof; and
- (b) a packaging cell line harboring at least one retroviral construct coding for proteins required for said retroviral vector to be packaged.
48. (Previously presented) An isolated host cell infected with a virion according to Claim 37.
- 49-51. (Canceled)
52. (Previously presented) A non-human host cell infected with a virion according to Claim 47.
- 53-54. (Canceled)
55. (Currently amended) A recombinant retroviral vector comprising, in operable linkage,
 - (a) retroviral vector DNA or at least a portion of the retroviral vector DNA comprising elements necessary for infection and direction of expression in target cells; and

- (b) one or more coding sequences which encode a naturally occurring therapeutic antimicrobial peptide or a biologically active derivative thereof, wherein the antimicrobial peptide or derivative thereof is selected from the group consisting of: cecropin, prececropin, preprocecropin, SB-37, Shiva-1, a part thereof, an analogue thereof, a homologue thereof a preform thereof, a preproform thereof, a biologically active peptide derived therefrom, and a combination thereof.
56. (Currently amended) A recombinant retroviral vector comprising in operable linkage,
- (a) a 5' long terminal repeat region comprising the structure U3-R-U5;
 - (b) one or more of said coding sequences wherein at least one sequence encodes for a naturally occurring therapeutic antimicrobial peptide or a biologically active derivative thereof, wherein the antimicrobial peptide or derivative thereof is selected from the group consisting of: cecropin, prececropin, preprocecropin, a part thereof, an analogue thereof, a homologue thereof a preform thereof, a preproform thereof, a biologically active peptide derived therefrom, and a combination thereof; and
 - (c) a 3' long terminal repeat region comprising a completely or partially deleted U3 region wherein said deleted U3 region is replaced by a polylinker sequence, followed by the R and U5 region to undergo promoter conversion.
57. (Previously presented) The recombinant retroviral vector according to Claim 56, wherein said polylinker sequence comprises at least one unique restriction site and, optionally, at least one insertion of a heterologous DNA fragment.

58. (Currently amended) A recombinant retroviral vector comprising in operable linkage,

- (a) a 5' long terminal repeat region comprising the structure U3-R-U5;
- (b) one or more coding sequences wherein at least one sequence encodes for a naturally occurring therapeutic antimicrobial peptide or a biologically active derivative thereof, wherein the antimicrobial peptide or derivative thereof is selected from the group consisting of: cecropin, prececropin, procecropin, a part thereof, an analogue thereof, a homologue thereof a preform thereof, a preproform thereof, a biologically active peptide derived therefrom and a combination thereof, and
- (c) a 3' long terminal repeat region comprising a completely or partially deleted U3 region wherein said deleted U3 region is replaced by a polylinker sequence which comprises at least one unique restriction site and at least one insertion of a heterologous DNA fragment which regulates the expression of at least one of the coding sequences of said vector, and comprises at least one or more elements selected from the group consisting of: regulatory elements and promoters.

59. (Previously presented) The recombinant retroviral vector according to Claim 57, wherein said heterologous DNA fragment encodes a peptide selected from the group consisting of marker peptides, therapeutic peptides, cell cycle regulatory peptides, tumor suppressor peptides, antiproliferation peptides and cytokines.

60. (Currently amended) A recombinant retroviral vector system comprising:

- (a) a recombinant vector comprising, in operable linkage,
 - (i) retroviral vector DNA or at least a portion of the retroviral vector DNA comprising elements necessary for infection and direction of expression in target cells; and

Serial No.: 08/999,690

- 2004 AUG 26 PM 2:28
- (ii) one or more coding sequences wherein at least one sequence encodes for at least one naturally occurring therapeutic antimicrobial peptide or a biologically active derivative thereof wherein the antimicrobial peptide or derivative thereof is selected from the group consisting of: cecropin, prececropin, preprocecropin, a part thereof, an analogue thereof, a homologue thereof a preform thereof, a preproform thereof, a biologically active peptide derived therefrom, and a combination thereof, and
 - (b) a packaging cell line harboring at least one retroviral construct coding for proteins required for said retroviral vector to be packaged.
61. (Previously presented) The recombinant retroviral vector system according to Claim 60, wherein said retroviral vector comprises, in operable linkage,
- (a) a 5' long terminal repeat region comprising the structure U3-R-U5;
 - (b) one or more of said coding sequences; and
 - (c) a 3' long terminal repeat region comprising a completely or partially deleted U3 region wherein said deleted U3 region is replaced by a polylinker sequence, followed by the R and U5 region to undergo promoter conversion.
62. (Currently amended) A retroviral particle produced by the recombinant retroviral vector system according to Claim [[60]] 61 after transfecting the packaging cell line with the retroviral vector system.
63. (Currently amended) A retroviral provirus produced by infection of target cells with a recombinant retroviral particle according to Claim 62 whereby the U3 sequence region duplicated during the process of reverse transcription in the infected target cell and appears in the 5' long terminal repeat and the 3' long terminal repeat of the resulting provirus, and the U5 of the 5' long terminal

Serial No.: 08/999,690

2011 AUG 26 PM 2:32

repeat duplicated during the process of reverse transcription in the infected target cell and appears in the 3' long terminal repeat and in the 5' long terminal repeat of the resulting provirus.

64. (Previously presented) The retroviral provirus of Claim 63 wherein said polylinker comprises heterologous DNA.
65. (Previously presented) A method for introducing nucleotide sequences into an isolated cell population comprising infecting the cell population with the recombinant retroviruses produced by the recombinant retroviral vector system according to Claim 60.

66-69. (Canceled)

70. (Currently amended) A mRNA of a retroviral provirus produced by infection of target cells with a recombinant retroviral particle from a recombinant retroviral vector system comprising:
 - (a) a recombinant vector comprising, in operable linkage,
 - (i) retroviral vector DNA or at least a portion of the retroviral vector DNA comprising elements necessary for infection and direction of expression in target cells; and
 - (ii) one or more coding sequences wherein at least one sequence encodes for at least one naturally occurring therapeutic antimicrobial peptide ~~or a biologically active derivative thereof~~ wherein the antimicrobial peptide ~~or derivative thereof~~ is selected from the group consisting of: cecropin, prececropin, preprocecropin, a part thereof, an analogue thereof, a homologue thereof ~~a preform thereof, a preproform thereof, a biologically active peptide derived therefrom, and a combination thereof~~, and

Serial No.: 08/999,690

- (b) a packaging cell line harboring at least one retroviral construct coding for proteins required for said retroviral vector to be packaged.
71. (Currently amended) A RNA produced by a vector wherein said vector comprises, in operable linkage,
- (a) retroviral vector DNA or at least a portion of the retroviral vector DNA comprising elements necessary for infection and direction of expression in target cells; and
 - (b) one or more coding sequences wherein at least one sequence encodes for at least one naturally occurring therapeutic antimicrobial peptide or a biologically active derivative thereof wherein the antimicrobial peptide or derivative thereof is selected from the group consisting of: cecropin, prececropin, preprocecropin, a part thereof, an analogue thereof, a homologue thereof, a preform thereof, a preproform thereof, a biologically active peptide derived therefrom, and a combination thereof.
72. (Previously presented) An isolated host cell infected with a virion according to Claim 62.

73-74. (Canceled)

75. (Previously presented) An isolated host cell infected with a virion according to Claim 62.

76-77. (Canceled)

Please add the following new claims:

78. (New) A recombinant retroviral vector comprising in operable linkage,
- (a) a 5' long terminal repeat region comprising the structure U3-R-U5;

Serial No.: 08/999,690

- 20TH AUG 24 1998
2000
- (b) one or more coding sequences wherein at least one sequence encodes for a therapeutic antimicrobial peptide, wherein the antimicrobial peptide is selected from the group consisting of: melittin, cecropin, magainin, a preform thereof, a preproform thereof, a biologically active peptide derived therefrom having antimicrobial activity, and a combination thereof; and
 - (c) a 3' long terminal repeat region comprising a completely or partially deleted U3 region wherein said deleted U3 region is replaced by a polylinker sequence, followed by the R and U5 region to undergo promoter conversion.
79. (New) A recombinant retroviral vector comprising in operable linkage,
- (a) a 5' long terminal repeat region comprising the structure U3-R-U5;
 - (b) one or more coding sequences wherein at least one sequence encodes for at least one therapeutic antimicrobial peptide, wherein the antimicrobial peptide is selected from the group consisting of: melittin, cecropin, magainin, a preform thereof, a preproform thereof, a biologically active peptide derived therefrom having antimicrobial activity, and a combination thereof; and
 - (c) a 3' long terminal repeat region comprising a completely or partially deleted U3 region wherein said deleted U3 region is replaced by a polylinker sequence which comprises at least one unique restriction site and at least one insertion of a heterologous DNA fragment which regulates the expression of at least one of the coding sequences of said vector, and comprises at least one or more elements selected from the group consisting of: regulatory elements and promoters.